provided a copy of Serial No. 60 019,639 herewith. Applicant responds below to each of the objections and or rejections set forth in the previous Office Action.

I. Enablement Under 35 USC §112, ¶1

Claims 33-38, 49-51, 57, and 63 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled. The Examiner states that the specification does not disclose how to use the instant invention, for example, for the curing of cancer *in vivo* in humans. According to the Examiner, it is not clear that reliance on the invention to cause tumor regression in mice of three tumor cells types accurately reflects the relative efficacy of the claimed therapeutic strategy in curing cancer in humans.

Applicant respectfully traverses. In order to support a *prima facie* enablement rejection, the burden is on the Patent Office to provide evidence or reasons why one skilled in the art could not make or use the claimed invention. Here, the Examiner has merely indicated that the invention possibly might not work in all circumstances. However, one skilled in the art, given the examples in the specification, would expect that the invention would also work in other circumstances, especially in view of the common mechanism involved.

In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

II. The Section 102 Rejection

Claims 1- 4, 6, 8-10, 12, 13, 20-22, and 52-53 stand rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Shi, *et al.*

In order to expedite prosecution and advance the case towards issuance, Applicant has provided a declaration (enclosed herewith as **Exhibit A**) which shows that the Shi et al. reference is not properly considered prior art to the present application under In re Katz, 215 U.S.P.Q. 14 (C.C.P.A. § 1982). The court in Katz states that "certainly one's own invention, whatever the form of disclosure to the public, may not be prior art against oneself, absent a statutory bar." Id at 454, citing In re Facius, 161 USPQ 294, 302; 408 F.2d 1396, 1406 (1969). In Katz, the inventor had co-authored an article, published it, and claimed that he was the sole inventor. The court found that the inventor's declaration that he was the sole inventor was sufficient to overcome the 102(a) rejection.

In the declaration, the inventor explained that the other authors were students working under his direction and supervision. This was enough to overcome an inference that the names were on the article because they were coinventors. "From such a relationship, joint inventorship cannot be inferred in the face of sworn statements to the contrary." Id. at 455. The court found that Dr. Katz had made a satisfactory showing that he was the sole inventor, and therefore his own work was not prior art under § 102(a).

Likewise, the publication of Applicant's co-authored paper should not be prior art because it is the work of the Applicant. The declaration states, under oath, that the authors who were not inventors were under the direction and supervision of the inventor, Yajun Guo. This provides a clear alternative to any inference that their names were on the article because they were coinventors. Thus, Applicant respectfully submits that the rejections based on the Shi et al. reference are improper and should be withdrawn.

In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

III. The Rejection of Claim 7

Claim 7 stands rejected under 35 U.S.C. §102(a) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as allegedly being obvious over Shi, *et al.*, as evidenced by *Rink*.

As noted above, Applicant has provided a declaration of the inventor under *In re Katz*, thereby removing Shi, *et al.* as a prior art reference. In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

IV. The Section 103 Rejection

Claims 1-4, 6-10, 12, 13, 20-22, 33-38, 49-54, and 63 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Wang, *et al.*, or Vanky, *et al.*, in view of Renner, *et al.*, or Bohlen, admissions in the Specification, Darlington, *et al.*, Chapoval, *et al.*, and Krummel, *et al.*

The Examiner originally argued that it would have been prima facie obvious to treat tumor cells with IFN-γ and TNF-α as taught by Wang or Vanky for the purpose of increasing the immunogenicity of the tumor cells by inducing expression of molecules like Class I MHC and

ICAM-1, and then to arm such tumor cells with bispecific antibodies that bridge the tumor cells to cytotoxic lymphocytes (CTLs) using bispecific antibodies such as those of Renner for the purpose of targeting CTL's to the cytokine-treated tumor cells and costimulating CTLs via binding of bispecific antibody to the CD28 receptor on CTLs. The Examiner also argued that one would have expected that such products would provide costimulation to CTLs via the free CD28 binding ligand and thus enhance the CTL activity (thereby ensuring the proliferation and stimulation of tumor-specific T cells) and that such products would be more immunogenic.

Applicant's previous arguments in essence explained that no proper motivation for combining the references had been provided and that even if combined the references failed to teach or suggest the claimed invention. To now expand on these points, Applicant notes that to merely state that one would combine the references

> for the purpose of targeting CTL's to the cytokine-treated tumor cells
> and costimulating CTLs via binding of bispecific antibody to the
> CD28 receptor on CTLs

fails to show how this motivation existed in the prior art and is not instead an improper hindsight reconstruction of the invention. Furthermore, even if one were to combine the cited references, the combined teaching still fails to teach or suggest the claimed composition comprising a target diseased cell and a bridge molecule or its claimed use. When viewed in context, rather than in hindsight, the combined teachings of the cited references at best merely amounts to the random , uncontrolled addition of components.

The Examiner's comments in the most recent Office Action appear to miss these major points, and instead focus on other additional arguments that were made. However, even with respect to these other issues, Applicant respectfully maintains that the Guo declaration and other arguments clearly demonstrate the non-obviousness of the present invention. In particular, Applicant's point regarding the Wang and Vanky references was and is that Wang and Vanky merely describe use of mixed lymphocyte-tumor cell cultures and thus fail to teach or suggest the use of an isolated autologous target diseased cell, as claimed. No has the Examiner explained why one skilled in the art, without the hindsight benefit of Applicant's specification, would modify the mixed culture of Wang or Vanky to instead use an isolated cell as in the present invention.

With respect to Chapoval (as well as Renner and Krummel) Applicant was merely explaining that these references describe adding bispecific antibodies to mixed lymphocyte-tumor cell cultures or directly into a patient and thus, without the benefit of improper hindsight, fail to teach or suggest adding such a bispecific antibody to a n isolated autologous target diseased cell, as claimed. Not has the Examiner explained what in the prior art, rather than Applicant's specification, would motivate one skilled in the art to so modify these references. It is unclear to Applicant what, if anything, the Examiner believes that Bohlen or Darlington add and or what the Examiner believes Applicant has admitted in the specification.

The Examiner criticizes item 4 of the Guo declaration on the grounds that the issue at hand is likely to be concentration dependence. However, to the extent the rejection is based on the personal knowledge of the Examiner, Applicant respectfully requests that a supporting affidavit be supplied in accordance with 37 C.F.R. §1.104(d)(2). Figure 6 of the Guo declaration is criticized for reflecting use of T-cells, but nothing in the method claims (which use the "comprising" transition) excludes the co-administration of T-cells. Finally the Examiner indicates that the claims do not exclude the generation of non or weakly immunogenic responses. However, the claims do require that the composition or method be useful for treating a patient.

In view of the above, Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

V. The Double-Patenting Rejection

Claims 1-4, 6-10, 12, 13, 20-22, 33-38, 49-54, 57, and 63 stand provisionally rejected under the judicially-created doctrine of obviousness-type double-patenting as allegedly being unpatentable over Claims 6, 7-9, 10, and 11 of co-pending Application No. 09/216,604.

Applicant respectfully requests that the Examiner hold this matter in abeyance until the claims in this Application are otherwise found allowable. Any further response at this time would be premature, as the claims in one or both of the Applications might change prior to issuance.

VI. Conclusion

For the foregoing reasons, it is respectfully submitted that the pending rejections are overcome, should be withdrawn, and that the claims are in full condition for allowance. If

clarification of any point discussed herein is needed to facilitate prosecution, the Examiner is invited to contact the undersigned at (858) 552-8400.

Please charge Deposit Account No. 12-2475 in the amount of $435.00 for the three-month extension of time due with this response. Applicant does not believe any other fees are due in connection with this submission, however if this is incorrect, please charge or credit Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,

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Dated: 6 July 2000

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